Elvucitabine

Drug Description

Elvucitabine is an L-cytosine nucleoside analogue.[1]

HIV/AIDS-Related Uses

Elvucitabine is a nucleoside reverse transcriptase inhibitor (NRTI) currently under investigation for the treatment of HIV infection and hepatitis B virus (HBV) infection.[2]

Non-HIV/AIDS-Related Uses

Elvucitabine has potent anti-HBV activity in laboratory studies. A Phase I/II study of elvucitabine in patients with chronic HBV infection demonstrated acceptable pharmacokinetics and safety. Phase II studies of elvucitabine in HBV infected patients are underway.[3]

Pharmacology

Elvucitabine is a beta-L-(-) nucleoside analogue developed to improve upon the antiviral activity of lamivudine, an FDA-approved beta-L-(-) nucleoside analogue. Elvucitabine is phosphorylated intracellularly to its 5'-triphosphate metabolite by cytoplasmic deoxycytidine kinase. Elvucitabine has a higher Km (substrate concentration at half maximum velocity) and a higher relative Vmax (maximum velocity) than deoxycitidine, whereas lamivudine has Km similar to deoxycitidine and a Vmax that is much lower than deoxycitidine's Vmax. Compared to lamivudine, elvucitabine may allow for less frequent dosing and escalation of dosage to overcome viral resistance.

The antiviral activity of elvucitabine has been shown to be 10- to 20-fold greater than that of lamivudine. Elvucitabine was tested in vitro against wild type HIV and 65 clinical strains of HIV with known nucleoside and non-nucleoside resistance mutations. Elvucitabine's 50% inhibitory concentration (IC50) against wild type and mutant HIV was 0.1 to 0.3 mM with one exception; the IC50 against M184V mutants was 1 to 4 mM.

Early clinical trials have demonstrated that elvucitabine also has potent antiviral activity in vivo, with mean viral load declines of 0.67 log10 to 0.78 log10 copies/ml.

Elvucitabine has excellent oral bioavailability and an intracellular half-life that exceeds 24 hours. It is being studied using once daily dosing.[4] [5] [6]

Adverse Events/Toxicity

Elvucitabine's L-nucleoside configuration may provide protection against mitochondrial toxicity, a serious side effect often seen with D-nucleosides. Mitochondrial deoxypyrimidine nucleoside kinase does not utilize elvucitabine as a substrate and early studies indicate that elvucitabine has no inhibitory effect on mitochondrial DNA synthesis at concentrations up to 10 mM.[7] [8]

Preliminary study results reported at the 12th International HIV Drug Resistance Workshop in June 2003 indicated that elvucitabine induced reversible bone marrow suppression. Six of 56 patients experienced myelosuppression while taking elvucitabine; four received 100 mg daily and two received 50 mg daily. Mild headache and gastrointestinal distress were also reported.[9]

Drug and Food Interactions

In vitro, elvucitabine exhibits synergistic antiviral activity with stavudine or zidovudine and additive antiviral activity with zalcitabine or didanosine.[10]

Clinical Trials

For information on clinical trials that involve Elvucitabine, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Elvucitabine AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[11]

Elvucitabine

Other Names

2,3-dideoxy-2,3-didehydro-beta-L-fluorocytidine[12]

beta-L-Fd4C[13]

ACH-126443[14]

ACH-126,433[15]

2,3-dideoxy-2,3-didehydro-beta-L-5-fluorocytidine[16]

L-Fd4C[17]

Further Reading

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Manufacturer Information

Elvucitabine
Achillion Pharmaceuticals
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New Haven, CT 06511
(202) 624-7000

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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